

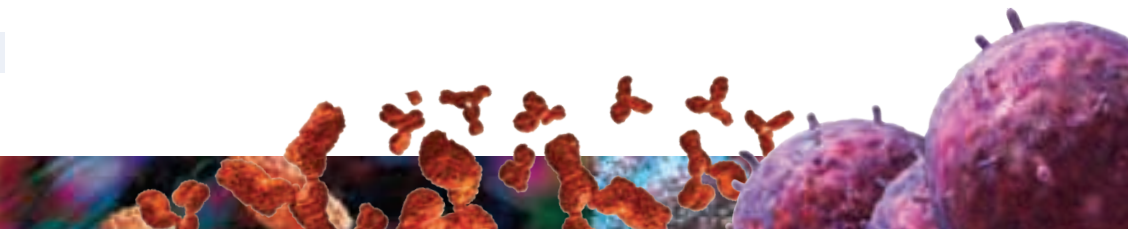
RECOMBINANT PROTEIN CONTRACT MANUFACTURING

Meridian Life Science, Inc. (MLS) is an industry leader in the commercial production of critical raw materials for the diagnostic market. MLS has a proven track record gained from over 25 years of cell culture, viral propagation, and protein purification experience. MLS has the expertise to develop and purify recombinant proteins from *E. coli*, yeast, insect or mammalian expression systems at research (mg) to commercial (g) scale. All manufacturing is performed following cGMP guidelines, with corresponding documentation and quality reviews.



WHY PARTNER WITH MLS?

- Unparalleled experience and proven track record (25+ yrs)
- Core expertise in cell culture, ascites, protein production and purification
- Flexibility in scale and production systems
- Complete R&D and Process Development service
- Dedicated project management
- All manufacturing conducted under ISO 9001:2008 and cGMP
- Complete confidentiality



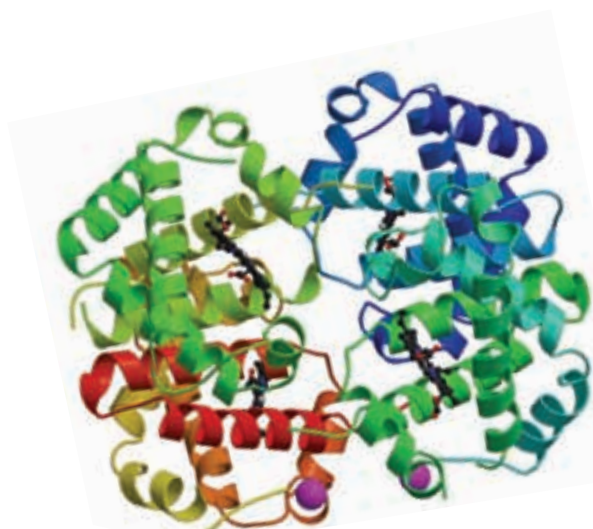
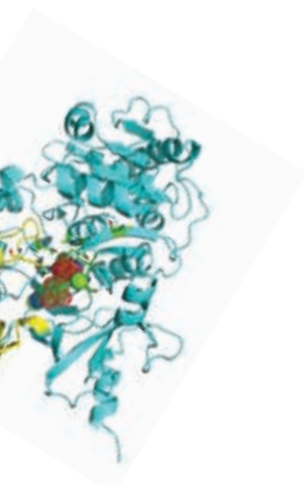
EXPRESSION SYSTEMS

E. coli: The most widely used expression system for recombinant proteins and capable of very high yield, fast growth and high density cell cultures. It is suitable for proteins that do not require post-translational modifications or regulated secretion.

Yeast: A stable expression system capable of generating post-translational modifications similar to mammalian expression. Advantages include high yield, high productivity, and significant cost and time savings over insect and mammalian expression systems.

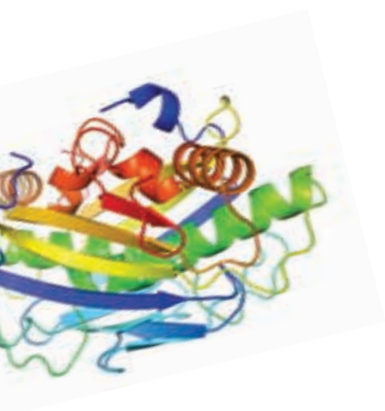
Insect: A robust system suited for the expression of large genes due to the powerful replication of baculovirus in insect cells and the strong polyhedral promoter. Can be readily adapted to high-density suspension culture for large-scale expression with protein yields from 30 to 500mg/L.

Mammalian: Generates the most comprehensive post-translational modifications for correct protein folding. Ideal for complex recombinant proteins, antibodies, virus, viral-subunit proteins, and gene-therapy vectors.



For More Information on Contract Manufacturing and Custom R&D Development; Contact a MLS Representative at contract-mfg@meridianlifescience.com.

R&D TO COMMERCIAL SCALE MANUFACTURING



PRODUCTION SYSTEMS

Tissue Culture Flasks | Spinner Flasks | Roller Bottles | Cell Factories | WAVE Bioreactors™ | Fermentors

CELL BANKING

MCB & WCB | Characterization

CULTURE CONDITION ANALYSIS - *Variable matrix analysis*

Cell density | Media optimization | Production system | Feed vs. batch mode | Physiological conditions

ANALYTICAL TESTING

SDS-PAGE (Variety of Stains) | Western Blot | UV-Vis Spectrophotometry | BCA/Bradford
HPLC Methods (RP, SEC, Other) | LAL Endotoxin | ELISA or other activity assay (Fluorescent Capabilities)

UPSTREAM OPTIMIZATION

DOWNSTREAM OPTIMIZATION

PRODUCTION

PURIFICATION METHODS

SEC, IEC, HIC, HyAP | Affinity columns | Centrifugation, Ultracentrifugation
Ultrafiltration, Dia-filtration, TFF (Plate or Hollow Fiber) | Formulation, Fill/Finish

EQUIPMENT

ÄKTAprime™ | ÄKTAexplorer™ | ÄKTApilot™ | ÄKTAready™

PURIFICATION PROCESS DESIGN - *Variable matrix analysis*

Harvest conditions | Lysis conditions | Clarification (Centrifugation / Filtration)
UF / DF | Chromatography | Precipitation

ANALYTICAL TESTING

SDS-PAGE (Variety of Stains) | Western Blot | UV-Vis Spectrophotometry
BCA/Bradford | HPLC Methods (RP, SEC, Other) | LAL Endotoxin
ELISA or other activity assay (Fluorescent Capabilities)

VALIDATION LOTS

Validate at scale
Regulatory requirements for commercial reagents

PILOT STUDY

Fixed-fee 1L, 5L, and 10L pilot studies

ROUTINE PRODUCTION

Flexible scheduling
Quotes on a per mg or gram basis



We understand that the variable nature of biological processes often requires ongoing R&D support. MLS has been and will continue to be a proactive partner to our clients, working to ensure that projects receive the technical expertise required for successful execution.

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RECOMBINANT PROTEIN DEVELOPMENT

E. COLI AND YEAST SERVICES

Sub-cloning	Sub-cloning into appropriate expression vector, analysis by sequence, restriction digest and plasmid maxi-prep
Expression and Evaluation	Transform into appropriate host strain (<i>S. cerevisiae</i> or <i>P. pastoris</i> for yeast)
Pilot Study and Optimization	Small scale culture and purification, QC by SDS-PAGE and Western Blot

BACULOVIRUS/INSECT CELL SERVICES

Sub-cloning	Sub-cloning into appropriate expression vector, analysis by sequence and restriction digest and plasmid maxi-prep
Expression and Evaluation	Transformation into appropriate host strain
Virus Generation	Generation of recombinant bacmid Transfection of insect cell with recombinant bacmid DNA Generation and titration of high titer viral stocks
Pilot Study and Optimization	Infection of insect cells with P3 stock Expression optimization and detection: MOI, time course, cell lines Small scale culture and purification, QC by SDS-PAGE and Western Blot

MAMMALIAN SERVICES

Sub-cloning	Sub-cloning into appropriate expression vector, analysis by sequence and restriction digest and plasmid maxi-prep
Expression and Evaluation	Transient transfection into appropriate host strain (CHO, HEK-293, etc.) OPTIONAL: Stable cell line development Protein expression level determined by ELISA or Western Blot
Pilot Study and Optimization	Small scale culture and purification, QC by SDS-PAGE and Western Blot

QUALITY SYSTEMS

Regulatory Affairs and Quality Assurance/Quality Control:

- Provide necessary support for R&D to cGMP production
 - Support tech transfer, batch records and release, and Certificate of Analysis
- ISO 9001:2008 certified

INFECTIOUS DISEASE ANTIGENS

MLS offers a comprehensive range of quality antigens for immunoassay development. Our expanding portfolio of native and recombinant antigens can be viewed online at www.MeridianLifeScience.com. Below is a representation of our key native and yeast recombinant antigens. These reagents can be used to test for the presence of antibodies to a specific target, or as calibrators and controls.

NATIVE ANTIGENS

7504 - CMV
7099 - CMV M
7095, 7517 - CMV EXT 2
7507 - CMV Grade III
9268 - CMV Grade II
7420 - EBV
8180 - EBV gp125
8198, 8505 - HAV
7305 - HSV-1
7705 - HSV-2
9287 - HSV-gG2
6119 - Rubella, Grade I
6075 - Rubella, Grade III
6076 - Rubella, Grade IV
8122 - Toxo
8131 - Toxo Grade III
7209 - VZV
8099 - Mumps
7844 - Rotavirus
7604 - Measles (Rubeola)
8175 - RSV

RECOMBINANT PROTEINS (YEAST)

VTI610 - Hepatitis B Core
VTI710 - Hepatitis C NP (p22)
VTI310 - HIV-1 gp41
VTI340 - HIV-1 p24
VTI360 - HIV-2 gp36
VTI520 - HSV-1 gG
VTI530 - HSV-2 gG
8198, 8505 - HAV
VTI510 - HSV-1 gD
VTI540 - HSV-2 gD
EV9298 - Rubeola



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